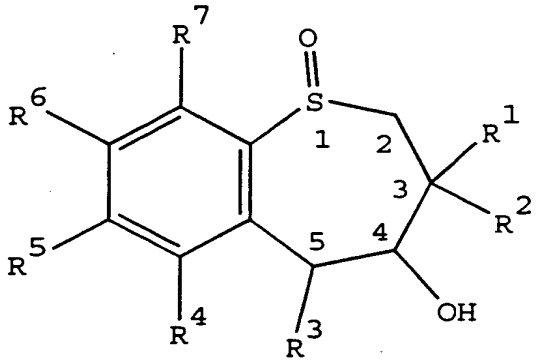
## CLAIMS

**What is claimed is:**

1. A method of preparing an enantiomerically-enriched tetrahydrobenzothiepine-1-oxide having the formula (I):



(I)

wherein:

$R^1$ and $R^2$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl;

$R^3$ is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, $OR^{24}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, and $SO_3R^{15}$,

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, $OR^{19}$, $NR^{19}R^{20}$, $SR^{19}$, $S(O)R^{19}$,

$SO_2R^{19}$, $SO_3R^{19}$, $NR^{19}OR^{20}$, $NR^{19}NR^{20}R^{21}$, $NO_2$, $CO_2R^{19}$, CN, OM, $SO_2OM$, $SO_2NR^{19}R^{20}$, $C(O)NR^{19}R^{20}$, C(O)OM, $COR^{19}$, $P(O)R^{19}R^{20}$, $P^+R^{19}R^{20}R^{21}A^-$, $P(OR^{19})OR^{20}$, $S^+R^{19}R^{20}A^-$, and $N^+R^{15}R^{17}R^{18}A^-$,

wherein:

$A^-$ is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation;

said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of $OR^{13}$, $NR^{13}R^{14}$, $SR^{13}$, $S(O)R^{13}$, $SO_2R^{13}$, $SO_3R^{13}$, $CO_2R^{13}$, CN, oxo, $CONR^{13}R^{14}$, $N^+R^{13}R^{14}R^{15}A-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, and $P(O)(OR^{13})OR^{14}$, and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, $NR^{13}$, $N^+R^{13}R^{14}A-$, S, SO, $SO_2$, $S^+R^{13}A-$, $PR^{13}$, $P(O)R^{13}$, $P^+R^{13}R^{14}A-$, or phenylene;

$R^{19}$, $R^{20}$, and $R^{21}$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, polyether, alkylarylalkyl, alkylheteroarylalkyl, alkylheterocyclealkyl,

heterocyclealkyl, heteroarylalkyl, quaternary heterocyclealkyl, alkylammoniumalkyl, carboxyalkylaminocarbonylalkyl, and quaternary heteroarylalkyl,

wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, $NR^{15}$, $N^+R^{15}R^{16}A^-$, S, SO, $SO_2$, $S^+R^{15}A^-$, $PR^{15}$, $P^+R^{15}R^{16}A^-$, $P(O)R^{15}$, phenylene, carbohydrate, amino acid, peptide, or polypeptide, and

$R^{19}$, $R^{20}$, and $R^{21}$ are optionally substituted with one or more groups selected from the group consisting of hydroxy, amino, sulfo, carboxy, sulfoalkyl, carboxyalkyl, sulfoalkyl, alkyl, heterocycle, heteroaryl, quaternary heterocyclealkyl, quaternary heteroarylalkyl, guanidinyl, quaternary heterocycle, quaternary heteroaryl, $OR^{15}$, $NR^{15}R^{16}$, $N^+R^{15}R^{17}R^{18}A^-$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, oxo, $CO_2R^{15}$, CN, halogen, $CONR^{15}R^{16}$, $SO_2OM$, $SO_2NR^{15}R^{16}$, $PO(OR^{22})OR^{23}$, $P^+R^{15}R^{16}R^{17}A^-$, $S^+R^{15}R^{16}A^-$, and C(O)OM,

wherein $R^{22}$ and $R^{23}$ are independently selected from the substituents constituting $R^{15}$ and M, or

$R^{20}$ and $R^{21}$, together with the nitrogen atom to which they are attached, form a cyclic ring;

$R^{24}$ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl;

$R^{13}$ and $R^{14}$ are independently selected from the group consisting of hydrogen and alkyl;

$R^{15}$ and $R^{16}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, carboxyalkyl, carboxyheteroaryl, carboxyheterocycle, carboalkoxyalkyl, carboalkylamino, heteroarylalkyl, heterocyclealkyl, and alkylammoniumalkyl; and

$R^{17}$ and $R^{18}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, $OR^{15}$, $NR^{15}R^{16}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, $CO_3R^{15}$, CN, halogen, oxo, and $CONR^{15}R^{16}$, wherein $R^{15}$ and $R^{16}$ are as defined above, or

$R^{17}$ and $R^{18}$ together with the nitrogen or carbon atom to which they are attached form a cyclic ring; and

$R^4$, $R^5$, $R^6$, and $R^7$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, halo, alkoxy, aryloxy, $-NO_2$, and $-NR^9R^{10}$;

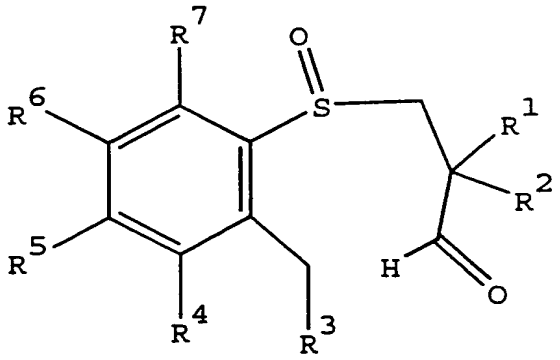
$R^9$ and $R^{10}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, butoxycarbonyl, and carbobenzyloxy;

$R^3$ and the hydroxyl at the 4-position of the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide are in a *syn*-conformation with respect to each other;

alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, and aryloxy can optionally be substituted with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, $-NO_2$, and halo; and

the sulfur at the 1-position of the seven-member ring and the carbons at the 4-position and the 5-position of the seven member ring are chiral centers;

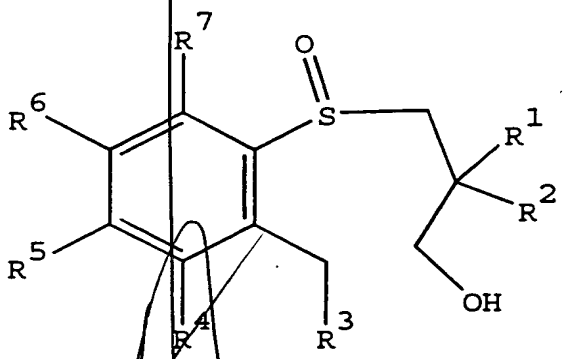
wherein the method comprises cyclizing an enantiomerically-enriched aryl-3-propanalsulfoxide having the formula (II):



(II)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and wherein the sulfur is an enantiomerically-enriched chiral center, to form the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide of formula (I).

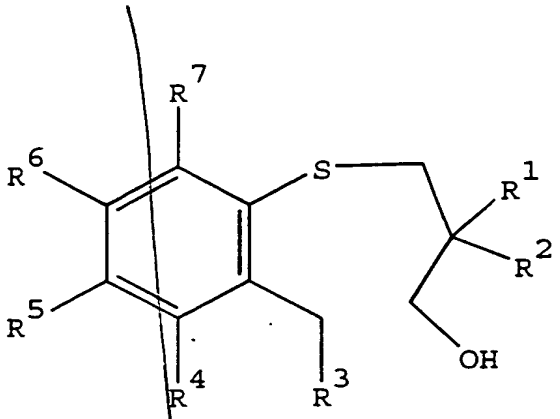
2. The method of claim 1 wherein the enantiomerically-enriched aryl-3-propanalsulfoxide of formula (II) is obtained by oxidizing an enantiomerically-enriched aryl-3-hydroxypropylsulfoxide having the formula (III):



(III)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described in claim 1, and wherein the sulfur is an enantiomerically-enriched chiral center, to form the enantiomerically-enriched aryl-3-propanalsulfoxide of formula (II).

3. The method of claim 2 wherein the enantiomerically-enriched aryl-3-hydroxypropylsulfoxide of formula (III) is obtained by oxidizing under enantioselective oxidation conditions an aryl-3-hydroxypropylsulfide having the formula (IV):



(IV)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described in claim 2, to form the enantiomerically-enriched aryl-3-hydroxy-propylsulfoxide of formula (III).

4. The method of claim 1 wherein said cyclizing is performed in the presence of a base.

5. The method of claim 4 wherein said base is potassium *t*-butoxide.

6. The method of claim 2 wherein the oxidation of the enantiomerically-enriched aryl-3-hydroxypropyl-sulfoxide is performed in the presence of sulfur trioxide pyridine complex.

7. The method of claim 2 wherein the oxidation of the enantiomerically-enriched aryl-3-hydroxypropyl-sulfoxide is performed in the presence of a pyridinium-chromium complex.

8. The method of claim 3 wherein the enantioselective oxidation conditions comprise a titanium (IV) alcoholate and a dialkyltartrate.

9. The method of claim 8 wherein the enantioselective oxidation conditions further comprise a hydroperoxide compound having the formula (V):

$$R^8\text{-}O\text{-}O\text{-}H \qquad (V)$$

wherein $R^8$ is a moiety selected from the group consisting of H, alkyl, carboalkyl, benzyl, benzoyl, and cumyl.

10. The method of claim 9 wherein $R^8$ is cumyl.

11. The method of claim 9 wherein $R^8$ is *tert*-butyl.

12. The method of claim 8 wherein the enantioselective oxidation conditions comprise titanium (IV) isopropoxide and diethyl-D-tartrate.

13. The method of claim 12 wherein the enantioselective oxidation conditions further comprise a hydroperoxide compound having the formula (V):

$$R^8\text{-}O\text{-}O\text{-}H \qquad (V)$$

wherein $R^8$ is a moiety selected from the group consisting of H, alkyl, carboalkyl, benzyl, benzoyl, and cumyl.

14. The method of claim 13 wherein $R^8$ is cumyl.

15. The method of claim 13 wherein $R^8$ is *tert*-butyl.

16. The method of claim 3 wherein the enantioselective oxidation conditions comprise a chiral (salen)metal complex and an oxidizing agent.

17. The method of claim 16 wherein the oxidizing agent is iodobenzene diacetate.

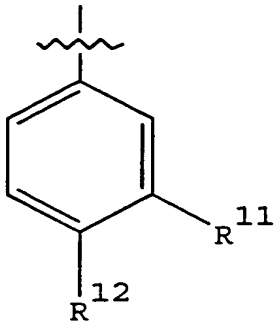
18. The method of claim 16 wherein the chiral (salen)metal complex is (S,S)-(+)-*N,N'*-bis(3,5-di-*tert*-butylsalicyclidene)-1,2-cyclohexanediaminomanganese (III) chloride.

19. The method of claim 3 wherein the enantioselective oxidation conditions comprise a chiral oxaziridine.

20. The method of claim 19 wherein the chiral oxaziridine is (1R)-(-)-(8,8-dichloro-10-camphor-sulfonyl)oxaziridine.

21. The method of claim 19 wherein the chiral oxaziridine is (1S)-(+)-(8,8-dichloro-10-camphor-sulfonyl)oxaziridine.

22. The method of claim 3 wherein $R^3$ has the formula (VI):



(VI)

wherein:

$R^{11}$ and $R^{12}$ are independently selected from the group consisting of alkyl, polyether, fluoride, chloride, bromide, iodide, $NR^{19}R^{20}$, $NR^{20}C(O)R^{19}$, and $OR^{19}$, wherein:

said alkyl and polyether can be further substituted with $SO_3R^{15}$, $N^+R^{15}R^{17}R^{18}A^-$, and quaternary heteroaryl;

$R^{19}$ is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, polyether, alkylarylalkyl, alkylheteroarylalkyl, alkylheterocyclealkyl, heterocyclealkyl, heteroarylalkyl, quaternary heterocyclealkyl, alkylammoniumalkyl, carboxyalkylaminocarbonylalkyl, and quaternary heteroarylalkyl;

said $R^{19}$ alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, $NR^{15}$, $N^+R^{15}R^{16}A^-$, S, SO, $SO_2$,

$S^+R^{15}A^-$, $PR^{15}$, $P^+R^{15}R^{16}A^-$, $P(O)R^{15}$, phenylene, carbohydrate, amino acid, peptide, or polypeptide;

$R^{19}$ is optionally substituted with one or more groups selected from the group consisting of hydroxy, amino, sulfo, carboxy, sulfoalkyl, carboxyalkyl, sulfoalkyl, alkyl, heterocycle, heteroaryl, quaternary heterocyclealkyl, quaternary heteroarylalkyl, guanidinyl, quaternary heterocycle, quaternary heteroaryl, $OR^{15}$, $NR^{15}R^{16}$, $N^+R^{15}R^{17}R^{18}A^-$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, oxo, $CO_2R^{15}$, CN, halogen, $CONR^{15}R^{16}$, $SO_2OM$, $SO_2NR^{15}R^{16}$, $PO(OR^{22})OR^{23}$, $P^+R^{15}R^{16}R^{17}A^-$, $S^+R^{15}R^{16}A^-$, and C(O)OM,

wherein $A^-$ is a pharmaceutically acceptable anion, and M is a pharmaceutically acceptable cation,

$R^{15}$ and $R^{16}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, carboxyalkyl, carboxyheteroaryl, carboxyheterocycle, carboalkoxyalkyl, carboalkylamino, heteroarylalkyl, heterocyclealkyl, and alkylammoniumalkyl;

$R^{17}$ and $R^{18}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, $OR^{15}$, $NR^{15}R^{16}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, $CO_3R^{15}$, CN, halogen, oxo, and $CONR^{15}R^{16}$, wherein $R^{15}$ and $R^{16}$ are as defined above, or

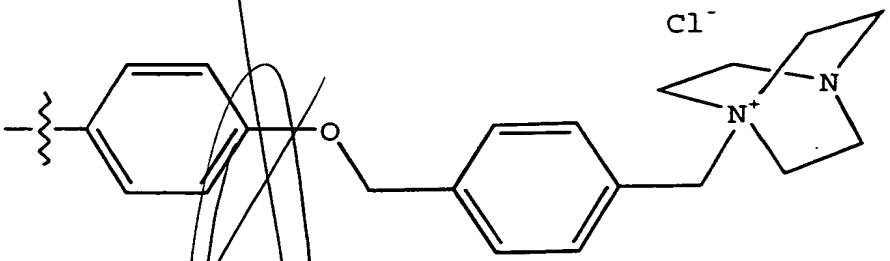
$R^{17}$ and $R^{18}$ together with the nitrogen or carbon atom to which they are attached form a cyclic ring; and

$R^{22}$ and $R^{23}$ are independently selected from the substituents constituting $R^{15}$ and M; and

$R^{13}$ and $R^{14}$ are hydrogen.

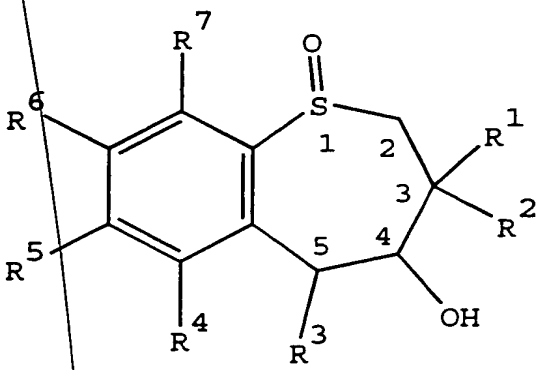
23. The method of claim 22 wherein $R^3$ is 4-methoxyphenyl.

24. The method of claim 22 wherein $R^3$ is a group having the structure of formula (IIa):



(IIa)

25. A method of preparing an enantiomerically-enriched tetrahydrobenzothiepine-1-oxide having the formula (I):



(I)

wherein:

$R^1$ and $R^2$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl;

$R^3$ is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, $OR^{24}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, and $SO_3R^{15}$,

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, $OR^{19}$, $NR^{19}R^{20}$, $SR^{19}$, $S(O)R^{19}$, $SO_2R^{19}$, $SO_3R^{19}$, $NR^{19}OR^{20}$, $NR^{19}NR^{20}R^{21}$, $NO_2$, $CO_2R^{19}$, CN, OM, $SO_2OM$, $SO_2NR^{19}R^{20}$, $C(O)NR^{19}R^{20}$, C(O)OM, $COR^{19}$, $P(O)R^{19}R^{20}$, $P^+R^{19}R^{20}R^{21}A^-$, $P(OR^{19})OR^{20}$, $S^+R^{19}R^{20}A^-$, and $N^+R^{15}R^{17}R^{18}A^-$,

wherein:

$A^-$ is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation;

said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of $OR^{13}$, $NR^{13}R^{14}$, $SR^{13}$, $S(O)R^{13}$, $SO_2R^{13}$, $SO_3R^{13}$, $CO_2R^{13}$, CN,

oxo, $CONR^{13}R^{14}$, $N^+R^{13}R^{14}R^{15}A^-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, and $P(O)(OR^{13})OR^{14}$, and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O, $NR^{13}$, $N^+R^{13}R^{14}A^-$, S, SO, $SO_2$, $S^+R^{13}A^-$, $PR^{13}$, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, or phenylene;

$R^{19}$, $R^{20}$, and $R^{21}$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, polyether, alkylarylalkyl, alkylheteroarylalkyl, alkylheterocyclealkyl, heterocyclealkyl, heteroarylalkyl, quaternary heterocyclealkyl, alkylammoniumalkyl, carboxyalkylaminocarbonylalkyl, and quaternary heteroarylalkyl,

wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, $NR^{15}$, $N^+R^{15}R^{16}A^-$, S, SO, $SO_2$, $S^+R^{15}A^-$, $PR^{15}$, $P^+R^{15}R^{16}A^-$, $P(O)R^{15}$, phenylene, carbohydrate, amino acid, peptide, or polypeptide, and

$R^{19}$, $R^{20}$, and $R^{21}$ are optionally substituted with one or more groups selected from the group consisting of hydroxy, amino, sulfo, carboxy, sulfoalkyl, carboxyalkyl, sulfoalkyl, alkyl, heterocycle,

heteroaryl, quaternary heterocyclealkyl, quaternary heteroarylalkyl, guanidinyl, quaternary heterocycle, quaternary heteroaryl, $OR^{15}$, $NR^{15}R^{16}$, $N^{+}R^{15}R^{17}R^{18}A^{-}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, oxo, $CO_2R^{15}$, CN, halogen, $CONR^{15}R^{16}$, $SO_2OM$, $SO_2NR^{15}R^{16}$, $PO(OR^{22})OR^{23}$, $P^{+}R^{15}R^{16}R^{17}A^{-}$, $S^{+}R^{15}R^{16}A^{-}$, and C(O)OM,

wherein $R^{22}$ and $R^{23}$ are independently selected from the substituents constituting $R^{15}$ and M, or

$R^{20}$ and $R^{21}$, together with the nitrogen atom to which they are attached, form a cyclic ring;

$R^{24}$ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl;

$R^{13}$ and $R^{14}$ are independently selected from the group consisting of hydrogen and alkyl;

$R^{15}$ and $R^{16}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, carboxyalkyl, carboxyheteroaryl, carboxyheterocycle, carboalkoxyalkyl, carboalkylamino, heteroarylalkyl, heterocyclealkyl, and alkylammoniumalkyl; and

$R^{17}$ and $R^{18}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl,

$OR^{15}$, $NR^{15}R^{16}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, $CO_3R^{15}$, CN, halogen, oxo, and $CONR^{15}R^{16}$, wherein $R^{15}$ and $R^{16}$ are as defined above, or

$R^{17}$ and $R^{18}$ together with the nitrogen or carbon atom to which they are attached form a cyclic ring;

$R^4$, $R^5$, $R^6$, and $R^7$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, halo, alkoxy, aryloxy, $-NO_2$, and $-NR^9R^{10}$;

$R^9$ and $R^{10}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, butoxycarbonyl, and carbobenzyloxy;

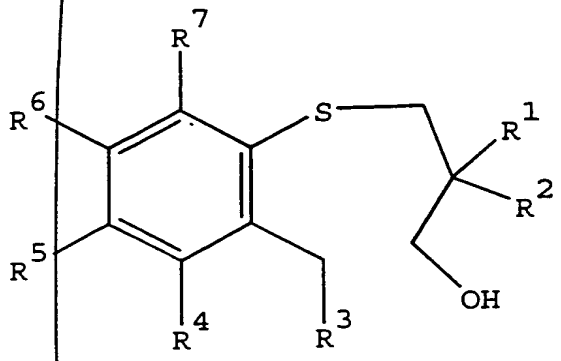
$R^3$ and the hydroxyl at the 4-position of the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide are in a *syn*-conformation with respect to each other;

alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, and aryloxy can optionally be substituted with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, $-NO_2$, and halo; and

the sulfur at the 1-position of the seven-member ring and the carbons at the 4-position and the 5-position of the seven member ring are chiral centers;

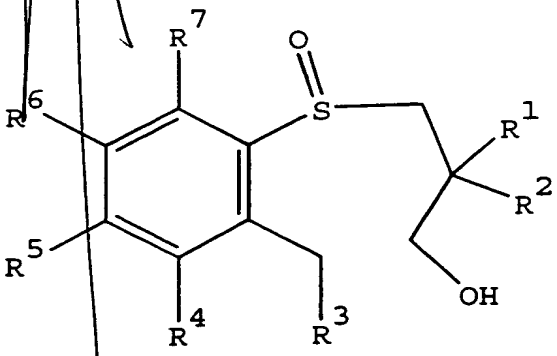
wherein the method comprises:

(a) oxidizing an aryl-3-hydroxypropylsulfide having the formula (IV):



(IV)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and wherein the oxidation is performed under enantioselective oxidation conditions to produce an enantiomerically-enriched aryl-3-hydroxypropylsulfoxide having the formula (III):

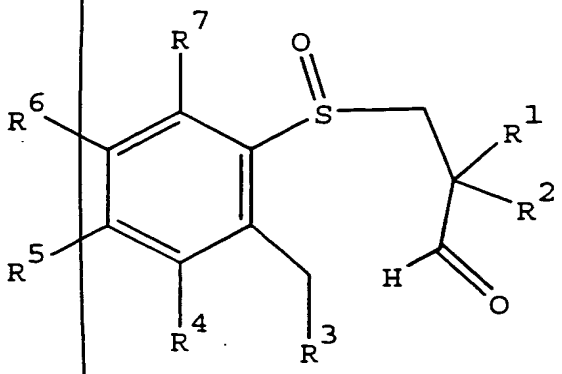


(III)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and the sulfur is an enantiomerically-enriched chiral center;

(b) oxidizing the 3-hydroxyl group of the enantiomerically-enriched aryl-3-hydroxypropyl-

sulfoxide to produce an enantiomerically-enriched aryl-3-propanalsulfoxide having the formula (II):



(II)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and the sulfur is an enantiomerically-enriched chiral center; and

(c) cyclizing the enantiomerically-enriched aryl-3-propanalsulfoxide to form the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide of formula (I).

26. The method of claim 25 wherein the enantioselective oxidation conditions comprise a chiral oxaziridine.

27. The method of claim 25 wherein the chiral oxaziridine is (1R)-(-)-(8,8-dichloro-10-camphor-sulfonyl)oxaziridine.

28. The method of claim 26 wherein the chiral oxaziridine is (1S)-(+)-(8,8-dichloro-10-camphor-sulfonyl)oxaziridine.

29. The method of claim 26 wherein the enantioselective oxidation conditions comprise a titanium (IV) alcoholate and a dialkyltartrate.

30. The method of claim 28 wherein the enantioselective oxidation conditions further comprise a hydroperoxide compound having the formula (V):

(V)

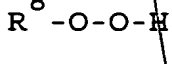
wherein $R^8$ is a moiety selected from the group consisting of H, alkyl, carboalkyl, benzyl, benzoyl, and cumyl.

31. The method of claim 30 wherein $R^8$ is cumyl.

32. The method of claim 30 wherein $R^8$ is *tert*-butyl.

33. The method of claim 29 wherein the enantioselective oxidation conditions of step (a) comprise titanium (IV) isopropoxide and diethyl-D-tartrate.

34. The method of claim 33 wherein the enantioselective oxidation conditions further comprise a hydroperoxide compound having the formula (V):



(V)

wherein $R^8$ is a moiety selected from the group consisting of H, alkyl, carboalkyl, benzyl, benzoyl, and cumyl.

35. The method of claim 34 wherein $R^8$ is cumyl.

36. The method of claim 34 wherein $R^8$ is *tert*-butyl.

37. The method of claim 25 wherein the enantioselective oxidation conditions of step (a) comprise a chiral (salen)metal complex and an oxidizing agent.

38. The method of claim 37 wherein the oxidizing agent is iodobenzene diacetate.

39. The method of claim 38 wherein the chiral (salen)metal complex is (S,S)-(+)-*N,N'*-bis(3,5-di-*tert*-butylsalicyclidene)-1,2-cyclohexanediaminomanganese (III) chloride.

40. The method of claim 25 wherein the oxidation of the enantiomerically-enriched aryl-3-hydroxypropylsulfoxide in step (b) is performed in the presence of sulfur trioxide pyridine complex.

41. The method of claim 25 wherein the oxidation of the enantiomerically-enriched aryl-3-hydroxypropyl-sulfoxide in step (b) is performed in the presence of a pyridinium-chromium complex.

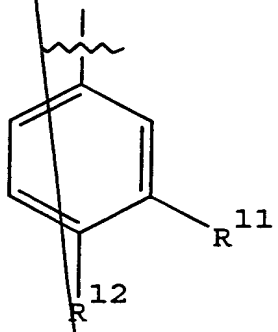
42. The method of claim 25 wherein the cyclizing of step (c) is performed in the presence of a base.

43. The method of claim 42 wherein the base is potassium *tert*-butoxide.

44. The method of claim 25 wherein $R^1$ and $R^2$ are moieties independently selected from the group consisting of ethyl and n-butyl.

45. The method of claim 25 wherein $R^1$ and $R^2$ are both n-butyl.

46. The method of claim 25 wherein $R^3$ has the formula (VI):



(VI)

wherein:

$R^{11}$ and $R^{12}$ are independently selected from the group consisting of H, alkoxy, $-NO_2$, $-NR^9R^{10}$, and $-OR^{10}$; and

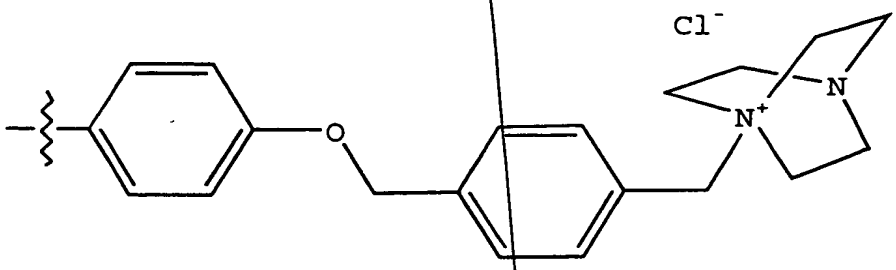
$R^9$ and $R^{10}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, butoxycarbonyl, and carbobenzyloxy, wherein aryl and heteroaryl can be optionally substituted with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, and halo.

47. The method of claim 46 wherein $R^1$ and $R^2$ are moieties independently selected from the group consisting of ethyl and n-butyl.

48. The method of claim 46 wherein $R^1$ and $R^2$ are both n-butyl.

49. The method of claim 48 wherein $R^{11}$ is H and $R^{12}$ is methoxy.

50. The method of claim 48 wherein $R^3$ is a group having the structure of formula (IIa):




(IIa)

51. The method of claim 25 wherein $R^4$, $R^5$, $R^6$, and $R^7$ are moieties independently selected from the group consisting of H, $-NO_2$, and $-NR^9R^{10}$.

52. The method of claim 51 wherein $R^4$, $R^6$, and $R^7$ are each H and $R^5$ is a moiety selected from the group consisting of $-NO_2$ and $-NR^9R^{10}$.

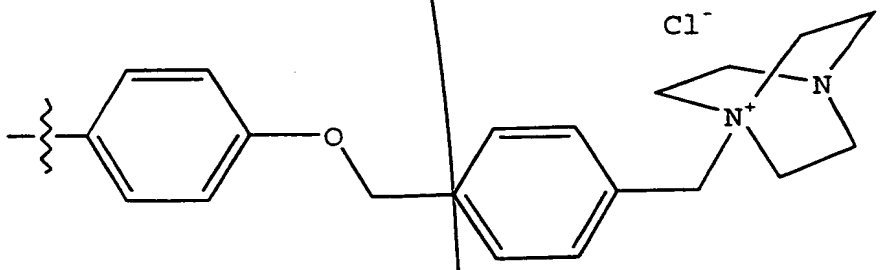
53. The method of claim 46 wherein $R^4$, $R^5$, $R^6$, and $R^7$ are moieties independently selected from the group consisting of H, $-NO_2$, and $-NR^9R^{10}$.

54. The method of claim 53 wherein $R^4$, $R^6$, and $R^7$ are each H and $R^5$ is a moiety selected from the group consisting of $-NO_2$ and $-NR^9R^{10}$.

55. The method of claim 53 wherein $R^5$ is dimethylamino.

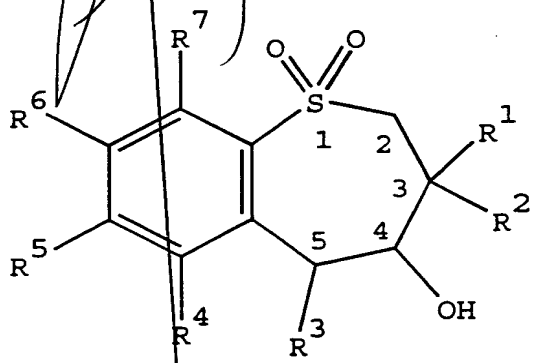
56. The method of claim 55 wherein $R^{11}$ is H and $R^{12}$ is methoxy.

57. The method of claim 55 wherein $R^3$ is a group having the structure of formula (IIa):



(IIa)

58. A method of preparing an enantiomerically-enriched tetrahydrobenzothiepine-1,1-dioxide having the formula (VII):



(VII)

wherein:

$R^1$ and $R^2$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heteroaryl;

$R^3$ is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, $OR^{24}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, and $SO_3R^{15}$,

wherein alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, quaternary heterocycle, and quaternary heteroaryl can be substituted with one or more substituent groups independently selected from the group consisting of alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, halogen, oxo, $OR^{19}$, $NR^{19}R^{20}$, $SR^{19}$, $S(O)R^{19}$, $SO_2R^{19}$, $SO_3R^{19}$, $NR^{19}OR^{20}$, $NR^{19}NR^{20}R^{21}$, $NO_2$, $CO_2R^{19}$, CN, OM, $SO_2OM$, $SO_2NR^{19}R^{20}$, $C(O)NR^{19}R^{20}$, C(O)OM, $COR^{19}$, $P(O)R^{19}R^{20}$, $P^+R^{19}R^{20}R^{21}A^-$, $P(OR^{19})OR^{20}$, $S^+R^{19}R^{20}A^-$, and $N^+R^{15}R^{17}R^{18}A^-$,

wherein:

$A^-$ is a pharmaceutically acceptable anion and M is a pharmaceutically acceptable cation;

said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can be further substituted with one or more substituent groups selected from the group consisting of $OR^{13}$, $NR^{13}R^{14}$, $SR^{13}$, $S(O)R^{13}$, $SO_2R^{13}$, $SO_3R^{13}$, $CO_2R^{13}$, CN, oxo, $CONR^{13}R^{14}$, $N^+R^{13}R^{14}R^{15}A-$, alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocycle, arylalkyl, quaternary heterocycle, quaternary heteroaryl, $P(O)R^{13}R^{14}$, $P^+R^{13}R^{14}R^{15}A^-$, and $P(O)(OR^{13})OR^{14}$, and

wherein said alkyl, alkenyl, alkynyl, polyalkyl, polyether, aryl, haloalkyl, cycloalkyl, and heterocycle can optionally have one or more carbons replaced by O,

$NR^{13}$, $N^+R^{13}R^{14}A^-$, S, SO, $SO_2$, $S^+R^{13}A^-$, $PR^{13}$, $P(O)R^{13}$, $P^+R^{13}R^{14}A^-$, or phenylene;

$R^{19}$, $R^{20}$, and $R^{21}$ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, polyalkyl, aryl, arylalkyl, cycloalkyl, heterocycle, heteroaryl, quaternary heterocycle, quaternary heteroaryl, polyether, alkylarylalkyl, alkylheteroarylalkyl, alkylheterocyclealkyl, heterocyclealkyl, heteroarylalkyl, quaternary heterocyclealkyl, alkylammoniumalkyl, carboxyalkylaminocarbonylalkyl, and quaternary heteroarylalkyl,

wherein alkyl, alkenyl, alkynyl, arylalkyl, heterocycle, and polyalkyl optionally have one or more carbons replaced by O, $NR^{15}$, $N^+R^{15}R^{16}A^-$, S, SO, $SO_2$, $S^+R^{15}A^-$, $PR^{15}$, $P^+R^{15}R^{16}A^-$, $P(O)R^{15}$, phenylene, carbohydrate, amino acid, peptide, or polypeptide, and

$R^{19}$, $R^{20}$, and $R^{21}$ are optionally substituted with one or more groups selected from the group consisting of hydroxy, amino, sulfo, carboxy, sulfoalkyl, carboxyalkyl, sulfoalkyl, alkyl, heterocycle, heteroaryl, quaternary heterocyclealkyl, quaternary heteroarylalkyl, guanidinyl, quaternary heterocycle, quaternary heteroaryl, $OR^{15}$, $NR^{15}R^{16}$, $N^+R^{15}R^{17}R^{18}A^-$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, oxo, $CO_2R^{15}$, CN, halogen, $CONR^{15}R^{16}$, $SO_2OM$, $SO_2NR^{15}R^{16}$, $PO(OR^{22})OR^{23}$, $P^+R^{15}R^{16}R^{17}A^-$, $S^+R^{15}R^{16}A^-$, and C(O)OM,

wherein $R^{22}$ and $R^{23}$ are independently selected from the substituents constituting $R^{15}$ and M, or

$R^{20}$ and $R^{21}$, together with the nitrogen atom to which they are attached, form a cyclic ring;

$R^{24}$ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, alkylammoniumalkyl, and arylalkyl;

$R^{13}$ and $R^{14}$ are independently selected from the group consisting of hydrogen and alkyl;

$R^{15}$ and $R^{16}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocycle, ammoniumalkyl, arylalkyl, carboxyalkyl, carboxyheteroaryl, carboxyheterocycle, carboalkoxyalkyl, carboalkylamino, heteroarylalkyl, heterocyclealkyl, and alkylammoniumalkyl; and

$R^{17}$ and $R^{18}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkenylalkyl, alkynylalkyl, heterocycle, carboxyalkyl, carboalkoxyalkyl, cycloalkyl, cyanoalkyl, $OR^{15}$, $NR^{15}R^{16}$, $SR^{15}$, $S(O)R^{15}$, $SO_2R^{15}$, $SO_3R^{15}$, $CO_3R^{15}$, CN, halogen, oxo, and $CONR^{15}R^{16}$, wherein $R^{15}$ and $R^{16}$ are as defined above, or

$R^{17}$ and $R^{18}$ together with the nitrogen or carbon atom to which they are attached form a cyclic ring;

$R^4$, $R^5$, $R^6$, and $R^7$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, halo, alkoxy, aryloxy, $-NO_2$, and $-NR^9R^{10}$;

$R^9$ and $R^{10}$ are independently selected from the group consisting of H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, butoxycarbonyl, and carbobenzyloxy;

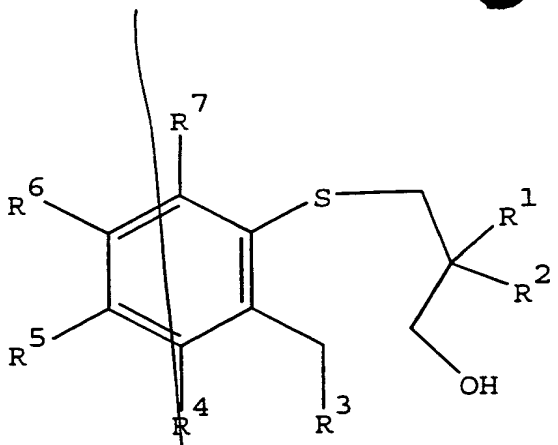
$R^3$ and the hydroxyl at the 4-position of the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide are in a syn-conformation with respect to each other;

alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, and aryloxy can optionally be substituted with one or more moieties selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, aryloxy, $-NO_2$, and halo; and

the carbons at the 4-position and the 5-position of the seven member ring are chiral centers;

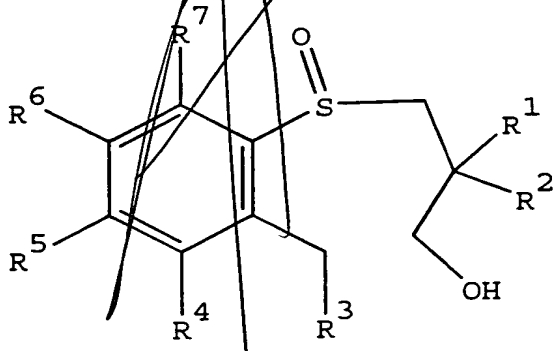
wherein the method comprises:

(a) oxidizing an aryl-3-hydroxypropylsulfide having the formula (IV):



(IV)

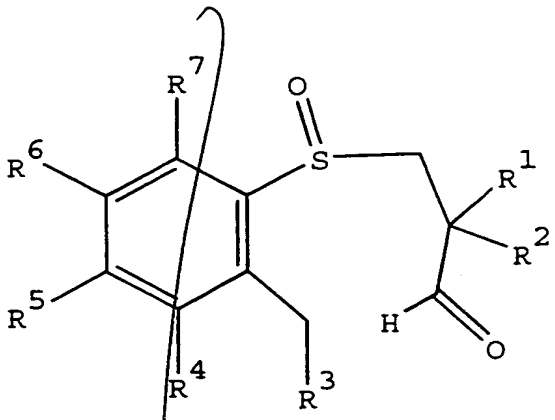
wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and wherein the oxidation is performed under enantioselective oxidation conditions to produce an enantiomerically-enriched aryl-3-hydroxypropylsulfoxide having the formula (III):



(III)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and the sulfur is an enantiomerically-enriched chiral center;

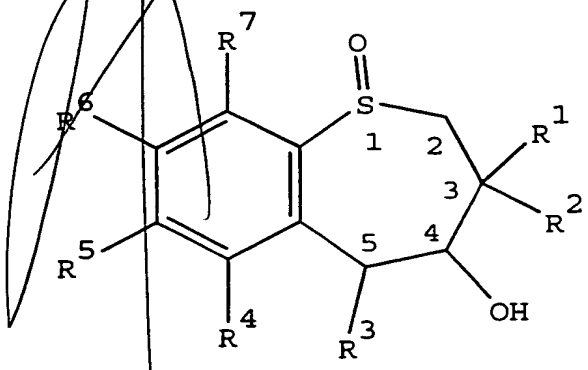
(b) oxidizing the 3-hydroxyl group of the enantiomerically-enriched aryl-3-hydroxypropyl-sulfoxide to produce an enantiomerically-enriched aryl-3-propanalsulfoxide having the formula (II):



(II)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above, and the sulfur is an enantiomerically-enriched chiral center;

(c) cyclizing the enantiomerically-enriched aryl-3-propanalsulfoxide to form an enantiomerically-enriched tetrahydrobenzothiepine-1-oxide having the formula (I):



(I)

wherein $R^1$, $R^2$, $R^3$, $R^4$, $R^5$, $R^6$, and $R^7$ are as described above and wherein $R^3$ and the hydroxyl group at the 4-position of the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide are in a *syn*-conformation with respect to each other, and the sulfur at the one-position of the seven-member ring and the carbons at the 4-position and the 5-position of the

seven member ring are enantiomerically-enriched chiral centers; and

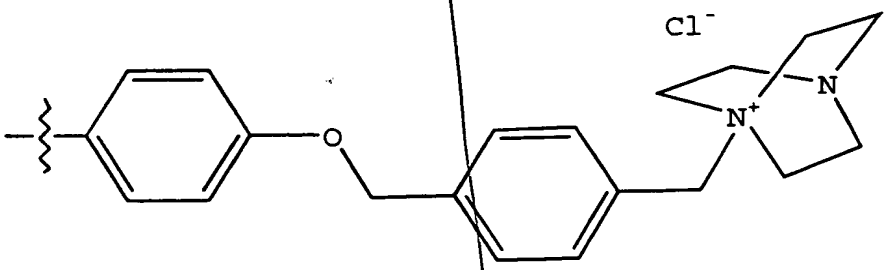
(d) oxidizing the enantiomerically-enriched tetrahydrobenzothiepine-1-oxide to the enantiomerically-enriched tetrahydrobenzothiepine-1,1-dioxide of formula (VII).

59. The method of claim 58 wherein the oxidizing of step (d) is performed in the presence of a peroxycarboxylic acid.

60. The method of claim 59 wherein the peroxycarboxylic acid is *m*-chloroperoxybenzoic acid.

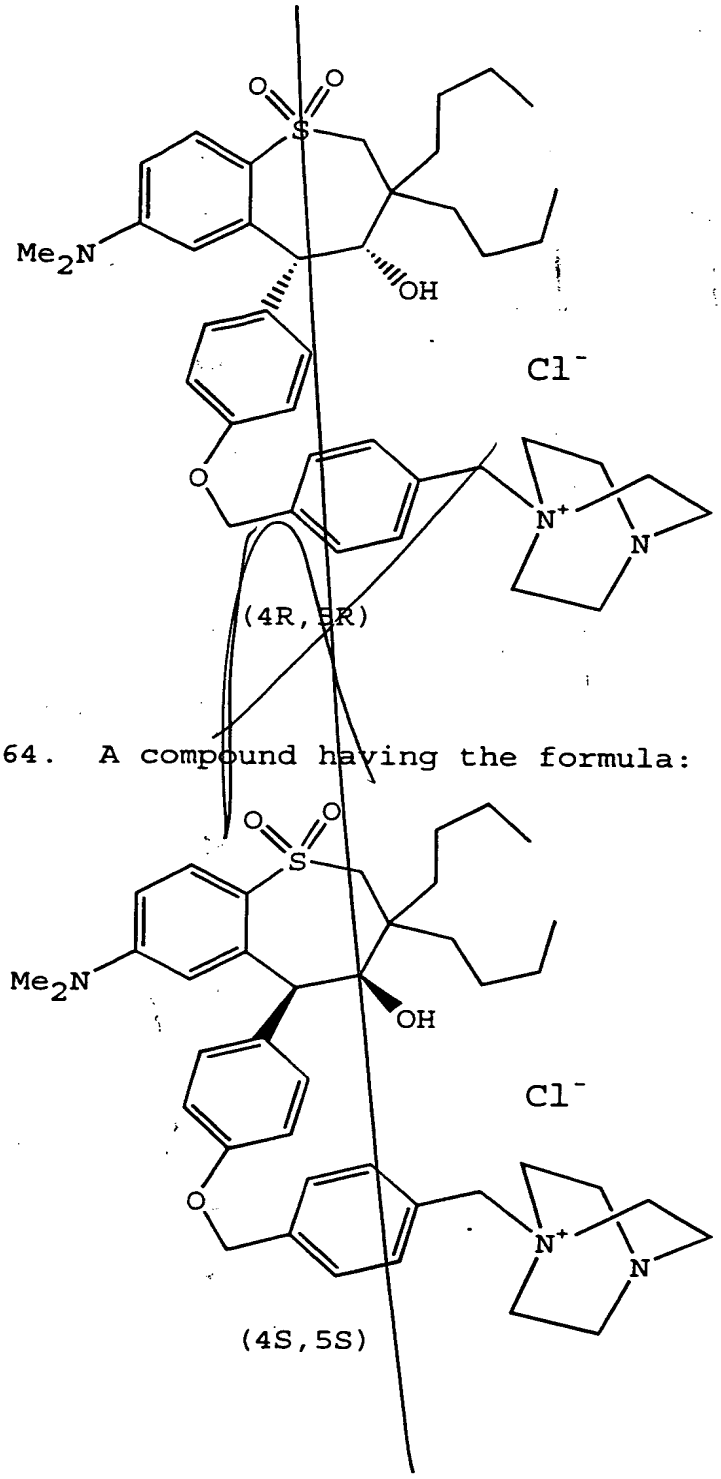
61. The method of claim 58 wherein $R^{11}$ is H and $R^{12}$ is methoxy.

62. The method of claim 58 wherein $R^{3}$ is a group having the structure of formula (IIa):




(IIa)

63. A compound having the formula:




((4R,5R)-XXVII)

64. A compound having the formula:




((4S,5S)-XXVII)